

REMARKS

Claims 1 and 12 have been amended to indicate that the antibodies of all claims are "monoclonal" and (for claim 12) "human" antibodies. Basis for using those terms can be seen throughout the Application (see, for example, the Abstract and the Summary of Invention at pages 3 and 4).

Claim 11 (and the Specification at page 11, lines 11 and 12) have been amended to indicate the ATCC Deposit Nos. (CRL 11306 and deposited March 24, 1993 and HB 11343 and HB 11344 deposited May 11, 1993). Enclosed herewith are true copies of the confirmations from the ATCC indicating that the cell lines have been deposited and accepted under the Budapest Treaty.

Formal Figures 12A through 12D are enclosed in response to the Notice of Draftsperson's Patent Drawing Review which was attached to the Official Action.

Re 35 USC 101 (Product of Nature):

Claims 1 - 10 and 12 - 14 were rejected under 35 USC 101 on the ground that, as written, the claims did "...not sufficiently distinguish over anti-TNF as it exists naturally." Reconsideration is requested. As can be seen, all claims are concerned with human and monoclonal antibodies that bind to human TNF alpha. The Applicants are the first to have been able to make a human anti-TNF antibody that binds specifically with human TNF. Human anti-TNF does not exist in nature. Therefore, reconsideration of the rejection under 35 USC 101 and reliance on the decision Diamond v. Chakrabarty, 206 U.S.P.Q. 193, is respectfully requested.

Re 35 USC 101 and 112 (Utility and Enablement):

The Specification and claims 1 - 10 and 12 - 14 were rejected under 35 USC 112 first paragraph on the grounds that the specification does not provide an enabling disclosure in that there is no indication of patentable utility for the claimed antibodies. Reconsideration is again requested. It is submitted that one skilled in the art would readily recognize the value of any monoclonal antibody directed to a specific substance such as TNF. The antibody has been shown to be able to bind to TNF. It is submitted that a demonstration of a mere binding of human anti-TNF alpha is sufficient demonstration of utility under the patent statute. At the very least, such binding would be useful in simple applications where one would want to use an antibody known to bind selectively with TNF (e.g., an immunoassay or purification step). See, for example, Table 1 on page 13 where the Applicants have demonstrated how far ^{anti} ^{antibodies} TNF can be diluted while still showing binding to ~~the cited human anti-TNF alpha antibodies~~. Therefore, reconsideration of the basis for rejection is respectfully requested.

Corrected as per
Applicants Request
in Paper # 4
PDB 4/12/94

Re 35 USC 112, first paragraph (the Cell Line Deposits):

Three of the cell lines used to express the human monoclonal antibodies of the invention have been deposited with ATCC under the Budapest Treaty, as shown on the enclosed deposit notice copies. The undersigned attorney of record hereby certifies that

- (1) the cell lines described on the enclosed ATCC notices have been accepted under the Budapest Treaty;
- (2) all restrictions upon public access to the deposits will be irrevocably removed upon the grant of a patent on this Application;
- (3) the deposits will be maintained for at least 30 years from the date of deposit or the enforceable life of the patent or the period of 5 years from the date of the most recent request for a deposit sample, whichever is longest; and
- (4) the deposits will be replaced if they become non-viable or non-replicable.

Re 35 USC 102:

Claim 12 was rejected under 35 USC 102(b) as being anticipated by Bringman, et al. With the above amendment to claim 12, it is submitted that this rejection should be withdrawn as the claims now clearly require the presence of a "human" monoclonal antibody. As can be seen by looking at the reference, it describes murine monoclonal antibodies. Thus, it is submitted the earlier rejection under 35 USC 102(b) is no longer proper and should be withdrawn.

Re 36 USC 103:

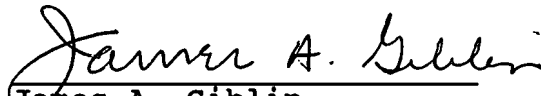
Claim 12 was also rejected under 35 USC 103 as obvious over Socher, et al. In view of the above amendments, it is submitted that this basis for objection should now be withdrawn since there is no indication that Socher, et al. discloses or suggests a human monoclonal antibody that binds to TNF alpha.

The Applicants appreciate the Examiner's recognition that claims 1 - 11 and 13 and 14 appear to be free of the prior art, and that the prior art does not recognize the existence of human auto-antibodies to human TNF.

In view of the above Amendments and Remarks, it is respectfully requested that the Examiner now find the claims to meet the requirements for patentability and issue a Notice for Allowance. If the Examiner responsible for this Application has any questions concerning the above Amendments or Remarks, that Examiner is invited to telephone the undersigned at any time.

Respectfully submitted,

Dated: December 22, 1993


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American Type Culture Collection

12301 Parklawn Drive • Rockville, MD 20852 USA • Telephone: (301)231-5520 Telex: 898-055 ATCCNORTH • FAX: 301-770-2587

BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT ISSUED PURSUANT TO RULE 7.3
AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10.2

To: (Name and Address of Depositor or Attorney)

Monte Wetzel
Miles, Inc.
P.O. Box 1986
Berkeley, CA 94701

RECEIVED

APR 06 1993

MILES INC.
BIOLOGICAL PRODUCTS
PATENT & LICENSING DEPT

Deposited on Behalf of: Monte Wetzel

Identification Reference by Depositor:

ATCC Designation

Human-Mouse heterohybridoma producing human IgM,
lambda anti-human TNF α , B5(F78-1A10-B5)

CRL 11306

The deposit was accompanied by: ☐ a scientific description ☐ a proposed taxonomic description
indicated above.

The deposit was received March 24, 1993 by this International Depository Authority and has been
accepted.

AT YOUR REQUEST:

☒ We will inform you of requests for the strain for 30 years.

The strain will be made available if a patent office signatory to the Budapest Treaty certifies one's
right to receive, or if a U.S. Patent is issued citing the strain.

If the culture should die or be destroyed during the effective term of the deposit, it shall be your
responsibility to replace it with living culture of the same.

The strain will be maintained for a period of at least 30 years after the date of deposit, and for a
period of at least five years after the most recent request for a sample. The United States and many
other countries are signatory to the Budapest Treaty.

The viability of the culture cited above was tested March 29, 1993. On that date, the culture was
viable.

International Depository Authority: American Type Culture Collection, Rockville, Md. 20852 USA

Signature of person having authority to represent ATCC:

Bobbie A. Brandon
Bobbie A. Brandon, Head, ATCC Patent Depository

Date: March 30, 1993

✓cc: Mr. Jim Giblin

Form BP4/9



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BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT ISSUED PURSUANT TO RULE 7.3
AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10.2

To: (Name and Address of Depositor or Attorney)

Miles Inc.
Attention: Monte Wetzel
P.O. Box 1966
Berkeley, CA 94701

Deposited on Behalf of: Miles Inc.

Identification Reference by Depositor:

ATCC Designation

Human-Mouse Heterohybridoma Producing Human IgG,K
Anti-human TNF α , F448-1D1-A8

HB 11343

Human-Mouse Heterohybridoma Producing Human IgM,
Anti-human TNF α , F80-1B9-F12

HB 11344

The deposits were accompanied by: ☐ a scientific description ☐ a proposed taxonomic description indicated above.

The deposits were received May 11, 1993 by this International Depository Authority and have been accepted.

AT YOUR REQUEST:

☒ We will inform you of requests for the strains for 30 years.

The strains will be made available if a patent office signatory to the Budapest Treaty certifies one's right to receive, or if a U.S. Patent is issued citing the strains.

If the cultures should die or be destroyed during the effective term of the deposit, it shall be your responsibility to replace them with living cultures of the same.

The strains will be maintained for a period of at least 30 years after the date of deposit, and for a period of at least five years after the most recent request for a sample. The United States and many other countries are signatory to the Budapest Treaty.

The viability of the cultures cited above was tested May 18, 1993. On that date, the cultures were viable.

International Depository Authority: American Type Culture Collection, Rockville, Md. 20852 USA

Signature of person having authority to represent ATCC:

Bobbie A. Brandon
Bobbie A. Brandon, Head, ATCC Patent Depository

Date: May 19, 1993

cc: Mr. Jim Giblin